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SENSITIZATION TO METABOLIC AND CARDIOVASCULAR EFFECTS OF CATECHOLAMINES

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16. Abstract

The mechanisms of sensitization to the cardiovascular and metabolic effects of catecholamine are studied. It is found that guanethidine increases the tensor response to noradrenaline by blocking its uptake, rather than by increasing the sensitivity of the alpha receptors. It is demonstrated that repeated injections of noradrenaline have no effect on the activity of the alpha receptors in response to a given stimulus. On the other hand, the sensitization of the beta receptors seems to be effected by other mechanisms: repeated injections of isoproterenol sharply increase the response to it: there is a 70% increase in oxygen, cardiac rhythm is elevated, and there is a strong increase in the contractile force of the ventricle. Repeated injections of isoprotererenol increase the sensitivity of the beta receptors, possibly by means of the cyclic AMP, while the sensitization of the alpha receptors would seem to be due simply to a diminution in uptake.

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SENSITIZATION TO METABOLIC AND CARDIOVASCULAR EFFECTS OF CATECHOLAMINES

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Our studies on the response of animals adapted to cold /255* to noradrenaline have led us to study the mechanisms of sensitization to the cardiovascular and metabolic effects of catecholamines. We first confirmed the importance of the "uptake" in the mechanism of sensitization at the level of the alpha receptors. Indeed, guanethidine increases the tensor response to noradrenaline by blocking the uptake, rather than by increasing the sensitivity of the alpha receptors. One could thus also demonstrate that repeated injections of noradrenaline have no effect on the activity of the alpha receptors in response to a given stimulus. The sensitization of the beta receptors seems to be effected by other mechanisms. Repeated injections of isoproterenol (300 µg/kg/day for 20 days), a pure beta stimulant, sharply increased the response to isoproterenol (INA). First, the increase of oxygen during the perfusion of INA (0.8 µg/kg/min) amounted to 70% in the animals treated with INA, as compared to 25% in the controls. Similarly, the elevation in cardiac rhythm in response to INA was 35 in the controls and 112 in the animals treated with INA. The drop in pressure caused by the vasodilation of IMA [sic] was less serious in the animals treated with INA than in the controls, probably because of differences in cardiac output. Indeed, chronic treatment with INA, in addition to causing a cardiac hypertrophy of about 40%, also sharply increases the contractile force of the ventricle. Thus repeated injections of INA increase the sensitivity of the beta receptors, possibly through the intermediary of the cyclic AMP, while the sensitization of the

*Numbers in the margin indicate pagination in the foreign text.

alpha receptors would seem to be due simply to a diminution in uptake, and it would not correspond to a real sensitization of the receptor.